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ORIGINAL ARTICLE

Meningiomas: skull base versus non-skull base

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Abstract

To identify differences between skull base meningiomas (SBM) and non-skull base meningiomas (NSBM). All adult patients (18.0–69.9 years) operated for intracranial meningiomas between 1990 and 2010 at our institution were investigated. Al-Mefty's definition was used to dichotomize tumors into SBM and NSBM. Overall, 1148 consecutive patients were identified. Median age at surgery was 54.2 years [18.1–69.9]. Median follow-up was 7.4 years [0.0–20.9]. There were 562 patients (49%) with SBM and 586 (51%) with NSBM. The two groups were similar with respect to patient age, follow-up time, and number of patients. Overall female-to-male ratio was 2.6:1, but 3.2:1 in SBM and 2.2:1 in NSBM ($p < 0.005$). With respect to presenting symptoms, SBMs had more often neurological deficits (risk ratio (RR) 1.4; $p < 0.0001$) and less often seizures (RR 0.4; $p < 0.0001$). Gross total resections were less frequent in SBM than NSBM (62 vs 84%) (RR 1.3; $p < 0.0001$). SBMs had a lower risk of WHO grades II and III histology (4.5 vs 9.5%) (RR 0.5; $p < 0.001$). Worsening of neurological function was more frequent in SBM (21 vs 121%) (RR 1.8; $p < 0.001$). Retreatment-free survival at 5, 10, and 15 years, respectively, was 80, 70, and 62% for SBM versus 90, 82, and 74% for NSBM ($p < 0.0001$). Overall survival at 5, 10, and 15 years, respectively, was 93, 85, and 78% for SBM and 96, 91, and 79% for NSBM ($p = 0.14$). Patients with SBMs had more new-onset neurological deficits and significantly shorter retreatment-free survivals, but this did not adversely affect the overall survival.

Keywords Craniotomy · Intracranial tumor · Meningioma · Retreatment-free survival · Overall survival

Introduction

According to the Central Brain Tumor Registry of the US (CBTRUS), meningiomas represent the most common primary brain tumor histology (36.6%) with an incidence rate of 8.03/100000 that increases with age, and a female-to-male ratio of 2.27 [34]. Histological grading is based on the current 2016 WHO classification [27] with overall proportions of WHO I, II (atypical), and III (anaplastic) intracranial meningiomas of 81.1%, 16.9%, and 1.7%, respectively [34].

Meningiomas are often asymptomatic and frequently incidental findings on MRIs performed. When symptomatic, the symptoms and signs are dependent on tumor location. Tumors over epileptogenic cortex often present with seizures, whereas skull base lesions more often present with cranial nerve deficits. Being a space-occupying lesion, all meningiomas can of course present with raised intracranial pressure (ICP).

Tumor location is of importance not only for presenting symptoms and signs, but also with respect to resectability and to prognosis. A subgroup of meningiomas is located, by convention, at the skull base. In lack of strict anatomical boundaries, there are many opinions as to what constitutes a skull base meningioma (SBM), but a commonly used definition can be found in the seminal book by Dr. Al-Mefty [15] (Table 1). Accepting this view, we propose to dichotomize the locations of meningiomas into SBM and non-skull base meningiomas (NSBM).

Surgical excision of the tumor and its dural base attachment is the most common primary mode of management [14, 17]. In 1957, Simpson [42] demonstrated the extent of resection (EOR) in intracranial meningiomas to strongly correlate with tumor recurrence in a 242-case series. However, the validity of the Simpson grade (SG) has been questioned in several studies. Recently, Nanda et al. [32] verified the system for both

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Table 1 Al Mefty's definition of skull base meningioma

1. Meningiomas of the anterior cranial base
A. Tuberculum sellae meningiomas
B. Olfactory groove meningiomas
C. Meningiomas of the orbital roof
2. Meningiomas of the middle cranial base
A. Meningiomas of the lateral and middle sphenoid wing
B. Meningiomas of the anterior clinoid
C. Meningiomas of the cavernous sinus
D. Meningiomas of the optic canal and orbit
E. Meningiomas of Meckel's cave
F. Cranio-orbital meningiomas
G. Meningiomas of the posterior clinoid and upper clivus
3. Meningiomas of the posterior cranial base
A. Clival meningiomas
B. Petroclival meningiomas
C. Sphenopetroclival meningiomas
D. Petrosal meningiomas
E. Anterior petrous meningiomas (petrous apex)
F. Posterior petrous meningiomas (CP angle)
G. Jugular foramen meningiomas
H. Tentorial meningiomas
I. Meningiomas of the temporal bone
J. Foramen magnum meningiomas

CP angle cerebellopontine angle

SBMs and NSBMs, but Voß et al. [48] found that SG is not equally prognostic in all locations in 2017 and claimed that the EOR has lower impact particularly for SBMs in the posterior fossa and falx meningiomas.

Lastly, SG I or II resections are not always achievable nor advisable due to the tumor location as gross total resection (GTR) may lead to catastrophic consequences [50] and several studies suggest that aggressive resections are associated with increased rates of new-onset neurological deficits, especially for SBMs [9, 13, 33].

The objective of this study is to identify differences between SBMs and NSBMs with the aim of providing new data on patient characteristics, presenting symptoms, outcomes, and retreatment rates after surgery.

Materials and methods

Clinical setting

Oslo University Hospital (OUH) consists of two neurosurgical units (OUH-Rikshospitalet and OUH-Ullevaal) and is a tertiary referral center with a catchment area of approximately three million inhabitants (56% of the Norwegian population).

Patient cohort

A total of 1148 consecutive adult patients (18.0–69.9 years old) who underwent craniotomies for intracranial meningiomas between 1990 and 2010 were investigated. Clinical information was retrospectively reviewed using patients' medical and surgical records from 1990 to 2002, whereas patient data from 2003 to 2010 were prospectively collected. Assessment of Karnofsky Performance Score (KPS) [20] was done using clinical records of preoperative visits. Patients' gender, age, and presenting symptoms (seizures, increased intracranial pressure, neurological deficits) were registered.

Tumor characteristics

The preoperative post-contrast imaging studies were reviewed to confirm tumor location, contrast enhancement, calcification, and size of the tumors. The EOR was assessed using the SG scale. CT scans and MRIs were also reviewed to confirm the degree of tumor removal. Each surgical case was approached attempting total tumor removal. The definition of SBM was based on Al-Mefty et al. [15] (Table 1), and thus, every intracranial lesion located elsewhere was considered a NSBM.

Outcome

All patients underwent follow-up for the assessment of outcomes. Neurological status at 6–12 months after surgery was trichotomized into unchanged, improved, or worsened and compared to preoperative status. Any reoperations for postoperative hematoma (extradural, subdural, intracerebral) and reoperation for postoperative infection (extradural, subdural, intracerebral, or infected bone flap) were recorded. Any retreatments for tumor recurrence by means of surgery, conventional fractionated radiotherapy (RT), or stereotactic radiosurgery (SRS) were also recorded. Surgical mortality was defined as death of any cause within 30 days of surgery [25]. Vital status (alive or dead) and time of death were obtained from the Norwegian Population Registry (Folkeregisteret) on 21 January 2011. Retreatment-free survival (RFS) was calculated from time of surgery to time of retreatment, time of death, or censoring. Overall survival (OS) was calculated from time of surgery to time of death or censoring.

Ethics

The study is regulated by the Personal Data Act/Personal Health Data Filing System Act and approved by the Data Protection Official at OUH (ePhorte 2017/5204). Informed consent is not required by the Personal Data Act/Personal Health Data Filing System Act.

Statistics

Univariate statistics were calculated without assuming a Gaussian distribution using the Wilcoxon test when the variable was continuous. With categorical variables, univariate statistics were calculated using the Pearson chi-squared test. In ordinal variables, the proportional odds likelihood test was used. Survival curves were generated using the Kaplan Meier estimator and the log-rank test was used to compare different survival curves. Relative risk ratios (RR) were calculated to estimate the strength of tumor location (SBM vs NSBM) and presenting symptoms, resection rates, neurological outcomes, and retreatment rates. The level of statistical significance was set at p value = 0.05. Descriptive statistics were reported as a median, mean, range, and 95% confidence interval (CI) if appropriate. JMP version 9 (SAS Institute Inc.) was used for all statistical analyses.

Results

Overall patient characteristics

We included 1148 patients with histologically verified intracranial meningiomas in our study (Table 2). Every patient underwent a craniotomy with resection and only one was lost to follow-up (moved abroad). Median follow-up was 7.4 years [range 0.0–20.9 years]. The overall patient characteristics are shown in Table 2.

Table 2 Overall characteristics

	n	%
Age (years)		
18–39	143	13
40–49	256	22
50–59	396	35
60–69	348	30
Sex		
Male	317	28
Female	831	72
Preoperative KPS		
≥ 70	1087	95
< 70	61	5
Presenting symptoms		
Asymptomatic	69	6
Seizures	350	30
Raised ICP	379	33
Neurological deficits	656	57
WHO grades		
WHO grade I	1062	93
WHO grade II	56	5
WHO grade III	24	2
Simpson grades		
Simpson grade I	442	39
Simpson grade II	399	35
Simpson grade III	61	5
Simpson grade IV	240	21
Simpson grade V	5	0
Retreatment		
Any retreatment	163	14
Surgery	102	9
Fractionated RT	48	4
Stereotactic RT	77	7

ICP intracranial pressure, *KPS* Karnofsky Performance Score, *RT* radiotherapy, *WHO* World Health Organization

Skull base versus non-skull base meningiomas

Five hundred sixty-two (49%) patients were affected by SBM and 586 (51%) had NSBM. The most common SBM locations were medial sphenoid wing (n = 100, 9%), tuberculum sellae/suprasellar (n = 81, 7%), and olfactory groove (n = 81, 7%) (Table 3). The most common NSBM locations were convexity (n = 280, 24%), parasagittal (n = 153, 13%), and falx (n = 132, 12%).

Age

Median age at surgery was 54.2 years [18.1–69.9]. There was no statistically significant difference between SBM and NSBM patients (p = 0.99) (Table 4).

Sex

The overall female-to-male ratio was 2.6:1, but 3.2:1 in SBM and 2.2:1 in NSBM (p < 0.005) (Table 4).

Preoperative KPS

Preoperative KPS was slightly lower in the SBM group compared to NSBM (median 80 vs 90; mean 81 vs 83; p < 0.005). Most of patients had a KPS ≥ 70 in both SBM and NSBM, but 34 SBM patients (6.1%) and 27 NSBM (4.6%) had a KPS < 70 (p = n.s.) (Table 4).

Presenting symptoms

With respect to presenting symptoms, SBMs had more often neurological deficits (RR 1.4; p < 0.0001) and less often seizures (RR 0.4; p < 0.0001), with no difference in raised ICP (p = 0.49) (Table 4).

Table 3 Tumor locations

	n	%
Skull base	562	49
Medial sphenoid wing	100	9
Olfactory groove	81	7
Tuberculum sellae/suprasellar	81	7
Lateral sphenoid wing	72	6
Cerebellopontine angle	66	6
Tentorium-intra	48	4
Petroclival	28	2
Tentorium-supra	22	2
Middle fossa/Meckel's cave	22	2
Intraorbital	15	1
Cavernosus sinus	14	1
Craniocervical junction/foramen magnum	13	1
Non-skull base	586	51
Convexity	280	24
Parasagittal	153	13
Falx	132	12
Intraventricular	21	2

WHO grades

Regarding WHO grades, 535 patients (95.2%) with SBM had a WHO grade I meningioma, 20 (3.6%) had WHO II, and 5 (0.9%) with a WHO III. Among NSBM patients, 527 (89.9%) were diagnosed with a WHO I meningioma, 36 (6.1%) with a WHO II, and 19 (3.2%) with a WHO III (Table 4). SBMs had a lower risk of WHO grades II and III histology (4.5 vs 9.3%) (RR 0.5; $p < 0.001$).

Simpson grade

In patients with SBMs, SG I was reached after surgery in 94 patients (17%), SG II in 256 (46%), SG III in 28 (5%), SG IV in 179 (32%), and SG V in only 5 (1%). Among patients with NSBM tumors, 348 (59%) achieved SG I, 143 (24%) SG II, 33 (6%) SG III, 61 (10%) SG IV, and no one underwent only biopsy (SG V). SG grade by location was highly statistically significant ($p < 0.0001$) (Table 4) and SBMs had a relative risk for subtotal resection (STR) (SG III–V) of 1.3 ($p < 0.001$).

Neurological outcome

In patients with SBMs, 219 (52%) were improved, 110 (27%) were unchanged, and 65 (21%) were worsened. In patients with NSBM tumors, 207 (58%) were improved, 119 (29%) were unchanged, and 69 (13%) were worsened. The difference was statistically significant ($p < 0.005$) (Table 4) and SBMs had a relative risk of worsened neurological outcome resection of 1.8 ($p < 0.001$).

Complications

The postoperative infection rate was lower in SBMs than in NSBMs (0.9% vs 4.1%) (RR 0.2; $p < 0.0005$), whereas the postoperative hemorrhage rates (1.8% vs 2.2%; $p =$ n.s.) and the 30-day mortality rates (1.6% vs 0.7%; $p =$ n.s.) were similar (Table 4).

Retreatment

In the SBM group, 109 (19%) underwent retreatment; surgery was performed in 61 patients (56%), 22 (20%) underwent fractionated RT, and 60 (55%) received SRS. In the NSBM group, 54 patients (9%) underwent retreatment; 41 (76%) received surgery, 26 (48%) fractionated RT, and 17 (31%) SRS. All retreatment bar SRS reached statistical significance (Table 4). SBMs had a relative risk for undergoing retreatment of 2.2 ($p < 0.001$), mostly by way of SRS.

The median time from primary surgery until any retreatment was 4.8 years (mean 5.5 years, range 3.7–9.0 years) for SBMs and 1.4 years (mean 1.8 years, range 0.6–4.5 years) for NSBMs ($p < 0.0001$).

Retreatment-free survival

Retreatment-free survival rates at 5, 10, 15, and 20 years, respectively, were 80, 70, 62, and 54% for SBM versus 90, 82, 74, and 70% for NSBM ($p < 0.0001$) (Table 4, Fig. 1). The difference in RFS was statistically significant ($p < 0.0001$).

Overall survival

Overall survival at 5, 10, 15, and 20 years, respectively, was 93, 85, 78, and 71% for SBM and 96, 91, 79, and 75% for NSBM ($p = 0.14$). The difference was not statistically significant (Table 4, Fig. 2).

Discussion

In this study, 1148 consecutive intracranial meningiomas operated at our institution between 1990 and 2010 were investigated to identify clinically relevant differences between SBMs and NSBMs with respect to epidemiology, presenting symptoms, treatment outcomes, and retreatment rate. Al-Mefty's definition was used to dichotomize tumors into SBM and NSBM (Table 1) [15].

Table 4 Skull base versus non-skull base

	Skull base *n* (%) 562	Non-skull base *n* (%) 586	*p* value
Age			
18–39 years	69 (12%)	74 (13%)	NS
40–49 years	121 (22%)	135 (23%)	
50–59 years	198 (35%)	198 (34%)	
60–69 years	174 (31%)	174 (31%)	
Sex			
Male	133 (24%)	184 (31%)	< 0.005
Female	429 (76%)	402 (69%)	
Preoperative KPS			
00	32 (6%)	57 (10%)	NS
90	201 (36%)	243 (42%)	
80	191 (34%)	177 (30%)	
70	104 (19%)	82 (14%)	
60	22 (4%)	14 (2%)	
50	6 (1%)	3 (0%)	
40	2 (0%)	7 (1%)	
30	3 (0%)	2 (0%)	
20	1 (0%)	1 (0%)	
Presenting symptoms			
Asymptomatic	28 (5%)	41 (7%)	NS
Symptomatic	534 (95%)	545 (93%)	NS
Seizures	102 (18%)	248 (42%)	< 0.0001
Raised ICP	180 (32%)	199 (34%)	NS
Neurological deficit	377 (67%)	279 (48%)	< 0.0001
WHO grades			
WHO grade I	535 (95%)	527 (90%)	< 0.0001
WHO grade II	20 (4%)	36 (6%)	
WHO grade III	5 (1%)	19 (3%)	
Simpson grade			
Simpson grade I	94 (17%)	348 (59%)	< 0.0001
Simpson grade II	256 (46%)	143 (24%)	
Simpson grade III	28 (5%)	33 (6%)	
Simpson grade IV	179 (32%)	61 (10%)	
Simpson grade V	5 (1%)	0 (0%)	
Neurological outcome			
Improved	219 (52%)	207 (58%)	< 0.005
Unchanged	110 (27%)	119 (29%)	
Worsened	65 (21%)	69 (17%)	
Complications			
Postoperative infection	5 (1%)	24 (4%)	< 0.0005
Postoperative hemorrhage	10 (2%)	13 (2%)	NS
30-day mortality	9 (2%)	4 (1%)	NS
Retreatment			
Any retreatment	109 (19%)	54 (9%)	
Surgery	61 (11%)	41 (7%)	< 0.05
Fractionated RT	22 (4%)	26 (4%)	NS
Stereotactic RT	60 (11%)	17 (3%)	< 0.0001
Retreatment-free survival			
5-year survival rate	80%	90%	< 0.0001
10-year survival rate	70%	82%	
15-year survival rate	62%	74%	
20-year survival rate	54%	70%	
Overall survival			
5-year survival rate	93%	96%	NS
10-year survival rate	85%	91%	
15-year survival rate	78%	79%	
20-year survival rate	71%	75%	

ICP intracranial pressure, *KPS* Karnofsky Performance Score, *NS* not significant, *RT* radiotherapy, *WHO* World Health Organization

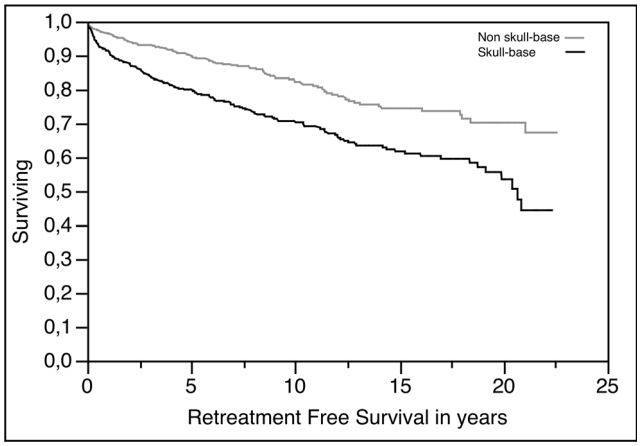

Fig. 1 Retreatment-free survival by meningioma location

Incidence

In our cohort, NSBMs were slightly more frequent than SBMs (51 vs 49%) (Tables 3 and 4). This finding is confirmed by many other authors [3, 7, 21, 22, 26], although in some cases, the discrepancy between the two macro-locations was greater than ours. Conversely, in case series by Bir et al. [4] and Nanda et al. [32], the amount of SBM patients was ≥ 65%, perhaps reflecting more specialized clinical practices or variations in the definitions of SBM.

Age

In this study, the median age of patients in NSBM and SBM groups was nearly the same (54.3 vs 54.2 years) and no significant difference was found (Table 4). In the literature, many SBM series [11, 14, 41, 44, 49] have lower median ages than NSBM cohorts [17, 31]. Hence, most of very old patients have more likely NSBMs. Given that, we excluded patients ≥ 70 years from this study, no significant discrepancy was detectable between the two groups. The median age of 58.3 years in our whole cohort is in line with what is reported in other studies [26, 32, 48, 52].

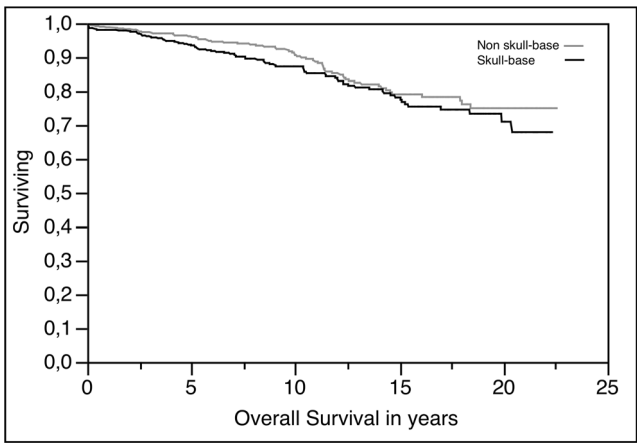

Fig. 2 Overall survival by meningioma location

Sex

Overall, the female-to-male ratio was 2.6:1 (Table 2), which is in accordance with data provided by CBTRUS [34]. It is well established in the literature that meningioma is a neoplasm that occurs more often in females, but different ratios are reported [3, 7, 26, 48, 52]. However, the female preponderance was more marked in SBM (3.2:1) than in NSBM (2.2:1) (Table 4). Our finding of a higher female-to-male ratio in SBMs is supported by several authors [14, 17, 31, 37, 41, 44].

Preoperative KPS

Preoperative KPS was similar in the two groups. KPS < 70 was found in 6% of the SBM patients ($n = 34$) versus 5% ($n = 27$) in the NSBM group (Table 4). Overall, the median KPS was 80, which is in accordance with the literature [7, 11, 41, 43].

Presenting symptoms

Seizures were twice as prevalent in patients with NSBMs as in the SBMs (NSBM 42% vs SBM 18%; RR 2.2; $p < 0.0001$) (Table 4). In a recent publication, Chen et al. [10] reported that NSBMs were more likely to be associated with preoperative seizures. In addition, they found that patients with neurological deficits as presenting symptoms had substantially reduced incidence of preoperative seizures. A finding of neurological deficits would indicate tumor location near the skull base and away from the neocortex. Thus, our results are in line with Chen et al. [10]. The incidence of preoperative neurological deficits in our study was higher in the SBM group and the difference was statistically significant ($p < 0.0001$). Interestingly, Chaichana et al. [7] found that headache, namely a symptom of mass effect, was inversely associated with preoperative seizures. In our study, on the other hand, both groups had almost the same number of patients with raised ICP and no significance was found (Table 4). Regarding the whole cohort, the large case series presented by Zouaoui et al. [52] had results which were very close to ours, apart from the rate of neurological deficits. Specifically, nearly 60% of our patients had neurological deficits, while Zouiaoui et al. [52] reported around half this number.

WHO grading

In our cohort, higher-grade meningiomas (WHO II and WHO III) were more frequent in the NSBM group (NSBM 10% vs SBM 4%; $p < 0.0001$) (Table 4). These results are supported

by prior studies that have demonstrated an increased risk of higher-grade meningiomas in the convexity location [24, 26, 30]. Kasuya et al. [22] reported that NSBM location is an independent risk factor for high MIB-1 staining index (≥ 3.0). An increased MIB-1 staining index is a common feature of higher-grade meningiomas, even though a certain amount of WHO I meningiomas has MIB-1 ≥ 3.0. Regarding SBMs, Scheitzach et al. [41] published values very similar to ours. Considering our entire series, the number of higher-grade meningiomas is in line with those reported by other authors [4, 21, 22].

Simpson grade

With respect to EOR, significantly, more patients in the NSBM group reached SG I or SG II (NSBM 84% vs SBM 62%) (Table 4). SBMs had a relative risk for STR (SG III-V) of 1.3 ($p < 0.001$). According to several recent publications, tumor location strongly correlates with SG [32, 35, 48]. However, GTR is far easier to achieve in patients with NSBMs, as demonstrated by Morokoff et al. [31] who achieved SG I in nearly 95% of cases. In a series of recurrent SBMs published by da Silva et al. [14], all cases but one had SG III or SG IV and the common surgical finding responsible for recurrence in that study was incomplete removal during the first surgery. However, attempting to achieve SG I for SBMs can be extremely challenging and can cause catastrophic vascular injury or disabling cranial neuropathies [50].

Complications to surgery

Quality of surgery is one of many factors that have an impact on OS. Thus, when addressing risk factors for OS, the quality of surgery should also be discussed. Surgical mortality, the rate of postoperative hematoma, the rate of deep postoperative infection, and neurological deterioration after surgery are all well-accepted indicators for quality of surgery.

Our data showed a significant difference in neurological outcome depending on the tumor location. SBMs had a relative risk for worsened neurological outcome resection of 1.6 ($p < 0.001$). Neurological outcome 6 months after surgery improved in 52% of SBM patients and worsened in 21%. In the NSBM group, 58% of the cases had improvement and 17% had a worsening (Table 4). This is in line with prior studies. Scheitzach et al. [41] reported a significant improvement of focal neurological deficit in 60.1% patients in a series of 226 SBMs. Overall, 64.6% cases showed a neurological improvement quantified using the Medical Research Council Neurological Severity Score (MRC-NPS) and 14.2% developed new neurological deficits during the follow-up period. Interestingly, the improvement rates differed significantly according to tumor location; tumors located at the foramen magnum had the worst outcome, while the best one was recorded for tumors of the lateral sphenoid wing and the olfactory groove.

Postoperative hematoma is a contributor to surgical mortality and morbidity. The rate for postoperative hematoma after craniotomy for tumor has been reported to be between 0.6 and 4% [2, 5, 8, 12, 17, 23, 25, 31, 36, 39]. Overall, 1.6% of the patients in our series were complicated with a hematoma that required reoperation, which is the lower end of that reported for meningiomas. We did not find a significant difference between SBM and NSBM (Table 4).

Postoperative infection causes morbidity, prolonged hospitalization, and increased costs. However, the long-term result with regard to survival and neurological outcome is less affected than after postoperative hematoma [8, 25]. The reoperation rate for deep infection after craniotomy for meningiomas ranges from 0.5 to 6.2% [6, 8, 25, 31, 39]. Overall, 2.6% of the patients in our series were complicated with a surgical site infection that required reoperation. Interestingly, the postoperative infection rate was lower in SBMs (0.9 vs 4.1%) (RR 0.2; $p < 0.0005$) (Table 4).

Retreatments

In our study, the overall retreatment rate was 14% (Table 4). This is in line with other authors, such as Voß et al. [48], who reported an overall recurrence rate of 13% after a median of 50 months' follow-up. Although retreatment rate is not synonymous with recurrence rate, the two are comparable. We prefer to use retreatment rather than recurrence, since not every recurrence necessarily leads to retreatment.

With respect to tumor location, the retreatment rate of SBMs was twofold that of NSBMs (RR 2.2; $p < 0.001$) (Table 4). This is in accordance with a recent publication by Scheitzach et al. [41], but contrasts that of Voß et al. [48] and others [1, 19] who did not find any correlation between recurrence and tumor location.

Radiotherapy and SRS

Overall, after recurrence, 4% of patients underwent conventional RT equally distributed between SBM and NSBM groups (Table 4). Regarding conventional RT, prior publications reported similar results [31, 41]. On the contrary, van Alkemade et al. [47] had a rate of conventional RT after tumor recurrence of 11.2%, much higher than that reported in our study.

In 7% of recurrences, SRS was chosen as the therapeutic option. Nearly 11% of SBM patients underwent SRS, compared to only 3% in the NSBM group (Table 4). This difference was highly significant ($p < 0.001$) with a relative risk of 3.9 for SBMs. Other authors reported similar recourse to SRS. In the WHO I meningioma series presented by Heald et al. [18], the overall recurrence rate was 14 and 9% of all patients

resorted to SRS. Similarly, Nanda et al. [32] reported treatment with SRS in 8% of patients with tumor recurrence. On the other hand, Morokoff et al. [31] published a case series of convexity meningiomas with only 1.2% of patients treated with SRS after recurrence.

Surgical retreatment

Overall, 9% of our patients underwent a second operation to treat tumor recurrence (Table 2). In the literature, various results are reported. In the case series published by Gallagher et al. [16], no recurrence was treated with surgery; 60% underwent SRS or fractionated RT, whereas 40% were followed up radiologically. Other authors presented values that were twofold compared to ours [1, 32]. In a study by Scheitzach et al. [41], 100% of recurrences in patients with SBMs underwent reoperation. Regarding NSBM tumors, 76% of patients were reoperated. This value is much higher than that reported by Morokoff et al. [31], even though the multiplicity of tumor recurrences was particularly sparse.

Retreatment-free survival

With respect to retreatment-free survival (RFS), we prefer using RFS rather than recurrence-free survival (RecFS) as the former is a more clinically relevant and robust parameter. In our series, we found a statistically significant relationship between tumor location and RFS (Table 4). SBMs had a significantly shorter median RFS than NSBMs (5.4 vs 6.0 years) (Fig. 1), and at 10 years, the RFS rates were 70 and 82%, respectively. Regarding SBMs, Savardekar et al. [40] reported a significantly higher progression rate as compared to NSBs. Although meningiomas at both locations paralleled each other with respect to tumor progression after 10 years, the trend highlighted in the first 10 years of follow-up reflects our findings. For NSBMs, our results are in line or better than previous reports for convexity meningiomas; Morokoff et al. [31] reported a RecFS of 90% and Hasseleid et al. [17] an RFS of 94% at 5 years.

With respect to RFS rates by EOR, the relationship between tumor location and RFS is hardly surprising given that the ability to achieve SG I resections varies greatly according to tumor position. Several authors reported a relationship between SG and RecFS [14, 28, 32, 51]. In mixed cohorts of SBMs and NSBMs, Mansouri et al. [28] found 10-year RecFS rates of 90 and 43% for GTR and STR, respectively. Similarly, Voß et al. [48] had a rate of recurrence of 12% for patients who underwent GTR compared to 20% for those who only received STR. In falcine and parasagittal meningiomas, Pettersson-Segerlind et al. [38] demonstrated that the recurrence rates increased with increasing SG and found the relative risk of recurrence in SG IV to be 1.8 compared to SG grades I–III. Further evidence supporting the correlation between the risk of recurrence and EOR has been provided by other authors [41, 48].

Regarding EOR and SBMs, Scheitzach et al. [41] obtained results similar to ours. In their series, the EOR correlated significantly with the time to recurrence ($p < 0.01$) and with a higher risk of recurrence in multivariate analyses ($p < 0.01$). However, this correlation might be unpredictable in meningiomas in certain SB locations. For instance, Talacchi et al. [46] presented a series of foramen magnum meningiomas in which 81% of patients underwent GTR and only one patient underwent reoperation. In their multicenter study, Voß et al. [48] found that only SG IV was significantly correlated with increased risk of retreatment in SBMs, whereas both SG III and SG IV were correlated with convexity meningiomas in multivariate analyses.

However, other authors have also questioned the superiority of a GTR in meningioma surgery. Voß et al. [48] concluded that in WHO I meningiomas, tumor control after STR with adjuvant RT was similar to GTR. These findings partially support the thesis of Sughrue et al. [45] who questioned the relevance of SG as a predictor of recurrence for WHO I meningiomas. However, Sughrue's findings were heavily criticized by Hasseleid et al. [17] who argued that their cohort was a mixture of SBM and NSBM meningiomas and that it was too small (only 77 convexity lesions) to underpin their conclusion. Hasseleid et al. [17] went on to demonstrate the relevance of the Simpson grading system for convexity meningioma WHO grade I. Later, van Alkemade et al. [47] and Nanda et al. [32] found significant associations between SG and recurrence rates of benign meningiomas, including SBM location.

Overall survival

We found no significant difference between SBM and NSBM with regard to OS (Table 4, Fig. 2), which is in accordance with both recent and older publications [29, 47]. Thus, even though patients with SBMs more frequently had STRs, more retreatments, and a shorter RFS, this did not translate into a reduced OS.

Conclusions

Patients with SBMs more frequently underwent retreatment and had significantly shorter RFS. However, there was no significant difference between SBMs and NSBMs with regard to OS.

Strengths and limitations of the study

The strengths of this study lie in the clinical setting, cohort size, and follow-up. The data were restricted to the two neurosurgical units performing these surgeries which are within a

geographically well-defined area, thereby reducing the possible confounding effect of differences in the access to health care services between health centers. Thus, we have avoided the selection bias inherently present in large multicenter studies. To our knowledge, this study represents the biggest series comparing SBMs with NSBMs. The series is consecutive and includes all craniotomies performed for histologically verifiable meningiomas within the study period in adult patients (18.0–69.9 years). The median follow-up was 7.4 years [range 0.0–20.9 years] and complete for all patients but one (moved abroad). The pre- and postoperative post-contrast imaging studies were reviewed to confirm tumor location and EOR. With respect to data quality, we used end points that are easily verifiable (i.e., 30-day mortality, reoperation for hematomas, and reoperations for infections). Neurological status was trichotomized (unchanged, improved, or worsened) to reduce the subjectivity of the observers. Lastly, we focused our attention on RFS and retreatment rate in order to provide practical information to surgeons.

However, this study is not free from limitations. First of all, due to the retrospective nature of our analysis, there are limitations in terms of data collection inherent in such studies, despite data from 2003 being collected prospectively. Pathology review was not performed, so the results are based on the original histopathology report and in accordance with the WHO criteria at the time of surgery. MIB-1 staining index or Ki67 was not available for the majority of the tumors and this parameter was therefore excluded from the study. The WHO criteria changed during the study period. From 1990 to 2001, the tumors were classified as benign, atypical, or anaplastic. The present WHO grading system for meningioma was implemented in 2001, which divides the tumors into grades I, II, and III. For this study, we reclassified the tumors operated before 2001 to the present WHO classification: benign = WHO grade I, atypical = WHO grade II, and anaplastic = WHO grade III.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required.

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